National Cancer Institute (NCI)
Knowledge Acquisition Session Report

Session Date: October 1, 1997 **Session Time:** 11:30 AM - 12:30 PM

Session Topic: Clinical Trial Data Management

Knowledge Analysts: Jennifer Brush, UTA (Lead); Christine DiNunzio, UTA

Organization: Lombardi Cancer Center, Georgetown University Hospital, Washington, D.C.

Session Location: Lombardi Cancer Center

Type of Session:

__X__ Interview _____ Task Analysis _____ Scenario Analysis
_____ Concept Analysis _____ Observation _____ Structured Interview
_____ Other: ____Tape_____

Documentation: Test Form

General Topic Area

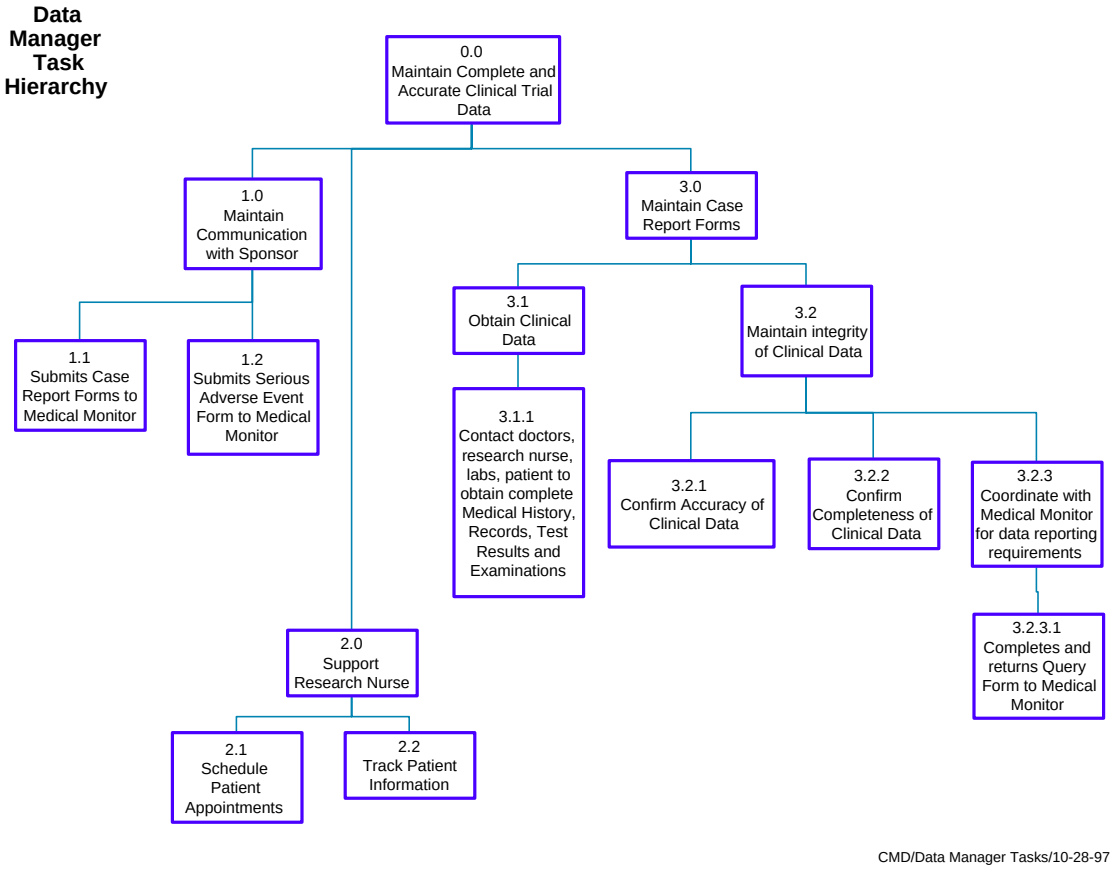
Clinical Trial Data Management

Session Objectives

Identify processes and procedures, information flows and problem areas for clinical data collection and storage during Breast Cancer Clinical Trials.

Report Summary

There are four to five Database Managers at the Lombardi Cancer Center (LCC) at Georgetown University Hospital. Each Data Manager works with a Research Nurse in the collection of data from Phase I, II and III Clinical Trials. Data Managers are responsible for clinical trial data collection and information flow between doctors, patients, drug companies and research nurses. Jennifer Bischoff is the Data Manager for Phase I trials. She reports to the Research Nurse responsible for Phase I Clinical Trials. Ruthie Kramer is the Data Manager for Breast Cancer trials. She reports to the Research Nurse responsible for Breast Cancer Clinical Trials. The report that follows was compiled from information gathered during a structured interview session.



Clinical Trial Data Collection

Overview

Case Report Forms (CRF) are used to record all clinical data obtained before, during and after a clinical trial. This data includes: patient information, patient medical history, exam results, lab results, clinical results, toxicity results, Serious Adverse Events (SAE) and post-trial follow up information.

Each clinical trial requires a unique set of Case Report Forms (CRFs). These forms are tailored to the reporting requirements outlined in the clinical trial protocol. Drug companies who are sponsoring a clinical trial provide unique CRFs to the participating institution(s). The National Cancer Institute (NCI) also provides unique CRFs for NCI sponsored trials. The Lombardi Cancer Center (LCC) uses their own unique CRFs when conducting internal clinical trials. The LCC is currently in the process of revising their internal CRFs.

Initiation Visits

After a Clinical Trial protocol has been approved - before the trial begins - an Initiation Visit takes place. This visit is one in which all the persons involved in the trial meet to review the protocol and discuss trial logistics. People typically attending this meeting include: the Principal Investigator, pharmacy nurse, drug sponsor representative (usually the CRA), the

Data Manager and the Research Nurse. (NOTE: it may be useful to attend one of these meetings for KA)

Clinical Trial Data
The Data Managers are responsible for filling out all CRFs for clinical trials conducted at LCC. The information used to fill out these forms is provided by the patient, physician and nurse observations, medical exams, lab results, and the patient medical record. Two complete sets of CRFs are maintained for each patient on a clinical trial. All of the information on the CRFs must be accurate and complete.

The Data Manager communicates with the patient, previous doctors, previous research institutions, the Primary Investigator (PI), the Research Nurse, lab technicians, and other Lombardi physicians and staff to obtain the clinical data necessary to complete the CRFs. This data collection process is the Data Manager's primary responsibility.

Clinical Trial Data can be divided into the following categories:

1. Pre-Clinical Trial Study Data
2. "On-Study" Clinical Trial Data
3. Serious Adverse Event (SAE) Reporting
4. Clinical Trial Monitoring
5. Clinical Trial Follow-up Data ("Off-Study")

1. Pre-Clinical Trial Study Data
Before an approved patient begins participation in a clinical trial, the Data Manager records a comprehensive patient profile. This profile includes:

- patient eligibility criteria
- complete medical history
- cancer history, lab forms
- tumor measurements
- copies of all pre-trial test results, (i.e. physical exams, eye exams, EKG, X-rays, CAT scans).

The Data Manager consults the patient, the patient's doctors, hospital personnel, and research institutions (if the patient has previously participated in a clinical trial) to obtain all of the medical data necessary to complete this comprehensive patient history. If there are additional data requirements or data clarification issues, the Data manager makes telephone inquiries to obtain information.

2. 'On-Study' Clinical Trial Data
The Data Manager is responsible for filling in all patient information on the Case Report Form on an ongoing basis. The Data Manager collects the required information from patients, doctors and the research nurse. Clinical Trial information includes: physical exam forms, progress form/notes, dispensing forms, medication records, lab results, medical records, and documentation of toxicity.

Ms. Bischoff noted that for the sake of quick reference, she maintains 'shadow' files (an abbreviated version of the complete medical record) for each patient. This is standard

practice in the research/clinical trial community. These shadow files include: research charts, visit schedule, medication schedule and dosage, lab results, patient reference numbers and site designation information.

3. Adverse Event (SAE) Reporting

A Serious Adverse Event (SAE) is when a patient experiences severe levels of toxicity, is hospitalized, or dies while on study (during the trial). When an SAE occurs, the Primary Investigator is required to complete and submit an SAE form within 24. The PI completes the SAE form and gives it to the Research Nurse. The RN then gives the form to the Data Manager.

The CRA for the drug company must be notified within 24 hours of the event. The Research Nurse, Data Manager or PI will call the CRA in the event of an SAE. The drug sponsor then completes a MEDWATCH form and submits it to the Institutional Review Board (IRB) of the research institution. The drug sponsor is also responsible for reporting the incident to the FDA.

If death occurs during a study, the patient consent form and the protocol may be adjusted - through the protocol review process - to reflect this new data.

Clinical Trial Monitoring

Medical Monitoring of a clinical trial takes place if a trial is sponsored by a drug company, NCI or other organization outside of the LCC.

The Data Manager coordinates with both a Medical Monitor and a CRA (Clinical Research Associate) during drug company sponsored clinical trials. The Medical Monitor is responsible for the periodic review of the Case Report Forms (CRF). Monitoring visits usually occur every four to six weeks. The Clinical Research Associate coordinates with both the Research Nurse and Data Manager regarding trial logistics and data collection requirements.

The Data Manager maintains two complete sets of CRFs. When a monitoring visit occurs, the Medical Monitor takes one set of CRFs back to the drug company where the clinical trial information is entered into the drug company database. If questions arise about data completeness or clarity, the drug sponsor submits a Query to the Data Manager. The Data Manager addresses the information / clarification request(s), completes the form and returns it to the Medical Monitor.

Clinical Trial Checklists—Breast Cancer

Ms. Kramer and her co-Data Manager on the Breast Cancer Clinical Trial team create customized forms for each Breast Cancer Clinical Trial. The doctors and nurses use these for evaluating patient symptoms and complaints. These forms are designed based on the attributes of each trial's protocol. These forms are maintained to facilitate data collection for the Case Report Forms and minimize follow-up from incomplete or unclear data.

The forms created for each Breast Cancer Clinical Trial are:

1. **Patient Eligibility Checklist:** This checklist details the requirements for patients' eligibility. The Data Manager generates this form using the guidelines outlined in the

Clinical Trial Protocol. The Data Manager then submits the form to the Research Nurse for use in subject screening interviews.

2. **Physical Exam Checklist:** This list details the expected symptom severity and toxicity levels for patients at each physical exam point during the Clinical Trial. The Data Manager generates this form using the guidelines outlined in the Clinical Trial Protocol. The Data Manager then submits the form to the attending doctor/nurse who will perform the physical exam.
3. **Follow-Up Visit Checklist**: This list details anticipated symptoms and reactions for each follow-up visit once the trial is complete. The institution conducts follow-up visits with patients once or on an ongoing basis, as specified in the Clinical Trial Protocol. The Data Manager generates this form using the guidelines outlined in the Clinical Trial Protocol. The Data Manager then submits the form to the attending doctor or nurse who performs the physical exam.

Clinical Data entered into the NCI database

The Data Manager is also responsible for providing clinical trial information to the data entry person. This person is responsible for entering clinical trial data into the NCI Database. The NCI database information categories and requirements are the same for all Clinical Trials at all research institutions.

Issues

- In the current NCI database, there is no place to make comments or to note abnormalities. The toxicity notes made by a doctor during a physical exam or required visit must be entered exactly as written. Patient complaints and symptoms often do not fit into the NCI criteria. Database categories are not case-specific. Frequently, reported patient symptoms must be left out and the reported clinical data does not reflect the full picture of patient reaction during the trial.
- The database operates from a baseline of patient status. If there is no change in a patient's symptoms over the course of a trial, then the symptoms are not reported and there is no reflection of possible side effects from the drug. (i.e. If a patient complains of headaches all through the trial, and there is no change in that symptom, then the symptom is not reported in the database.)
- The patient usually sees different doctors for each physical exam and required visit. There is no standardization of reporting patient symptoms or complaints, so what may be a severe headache to one doctor is mild to another. Or if a patient indicated a symptom during one visit, which was noted in the physical exam report, the doctor the patient sees on the next visit may not follow up on the progress of that symptom. The Data Manager suggested that a standardization of reporting symptoms would facilitate Clinical Trial data reporting.
- The database is uncorrectable. If the data entry person makes an incorrect entry, it cannot be changed.
- Standardization of Clinical Trial Checklists (could be used in all Clinical Trials).
- Standardization of "normals," (level of symptom severity) for all research institutions. Currently, each institution determines their individual standard of "normals.".

Entries for Domain Dictionary

Case Monitors: drug sponsor representative responsible for collecting the Case Report Forms from the Data Manager and coordinating data collection questions with the research institution (also called Medical Monitor)

Case Report Forms: forms created by the drug company or sponsoring institution, sometimes specific to each clinical trial, for the recording and collection of patient data prior to, during and after a Clinical Trial

Data Manager: person at the research institution responsible for data collection and integrity during a clinical trial; maintains Case Report Forms

IRB (Institutional Review Board): An elected committee of local physicians and laypersons, serving two year terms, who approve the initiation of and conduct periodic review of, biomedical research involving human subjects. The primary purpose of this board is to assure the protection of the rights and welfare of the human subjects.

LCC: Lombardi Cancer Center, Georgetown University Hospital

MEDWATCH: form used to report a Serious Adverse Event

Medical Monitor: drug sponsor representative responsible for collecting the Case Report Forms from the Data Manager and coordinating data collection questions with the research institution (also called Case Monitor)

SAE (Serious Adverse Event): hospitalization, death or toxicity of patient while on study (during a clinical trial)